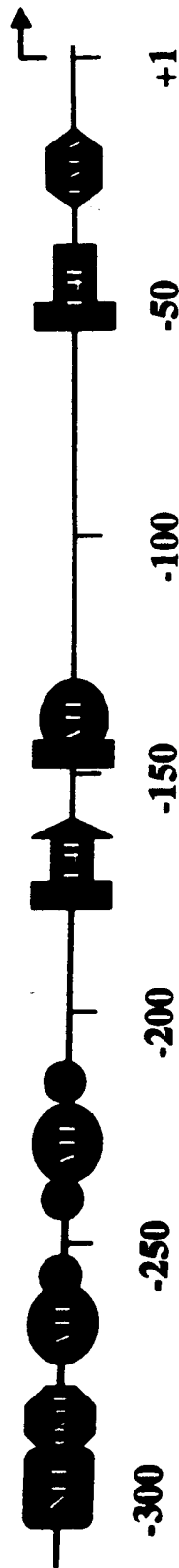


FIGURE 1



Symbol Legend:










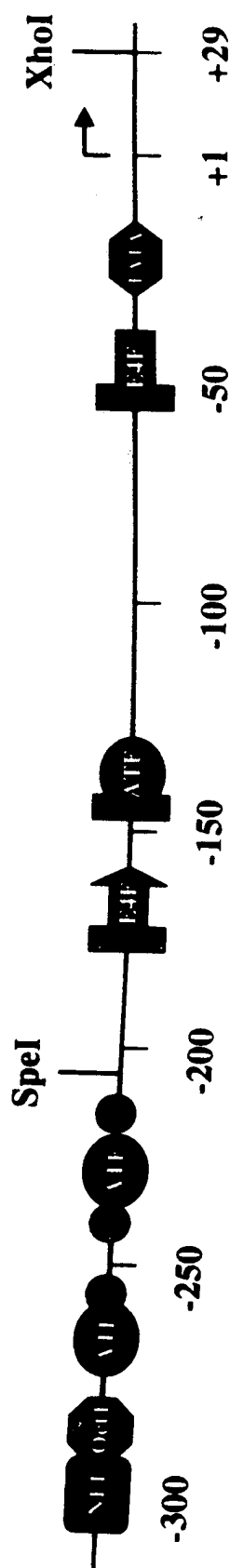
- | | | | |
|---|---|--|---|
|  | NF-1 binding site centered around -300 |  | EivF binding sites near -165 and -50 |
|  | Oct1 binding site positioned near -285 |  | E4TF1 binding site positioned around -140 |
|  | ATF binding sites near -260, -230, and -140 |  | TATA box positioned near -30 |
|  | Sp1 binding sites near -255, -240, and -220 |  | transcriptional start site denoted as +1 |
|  | E4F inverted repeat binding sites near -165 and -50 | | |

FIGURE 2

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Nucleotide Alterations

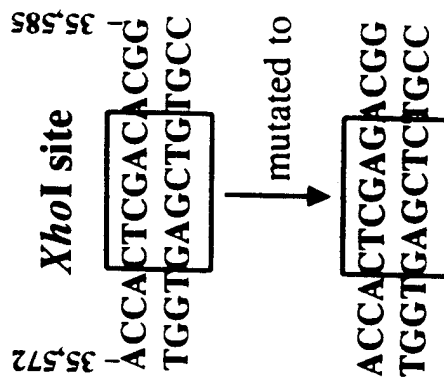
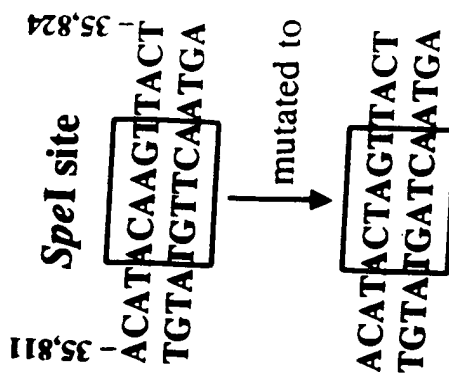
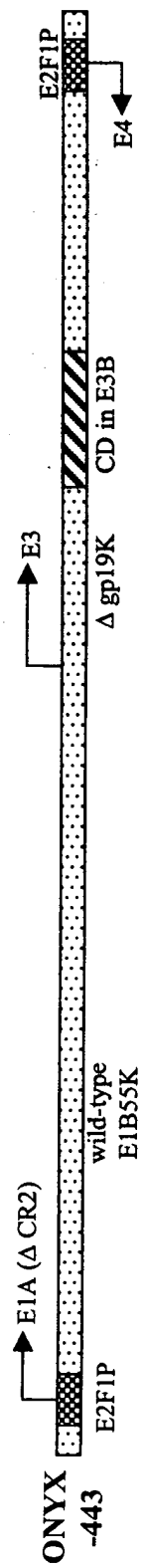


FIGURE 3

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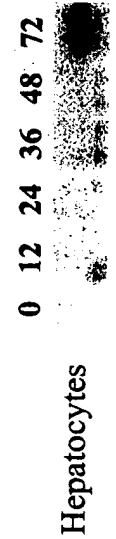
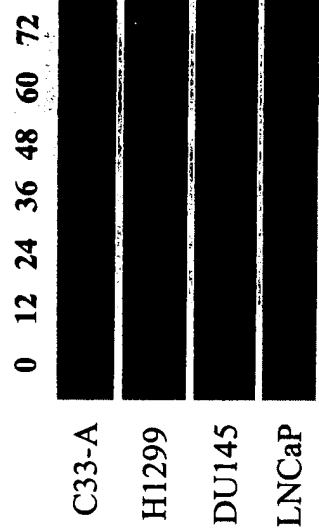
Figure 4.

A.



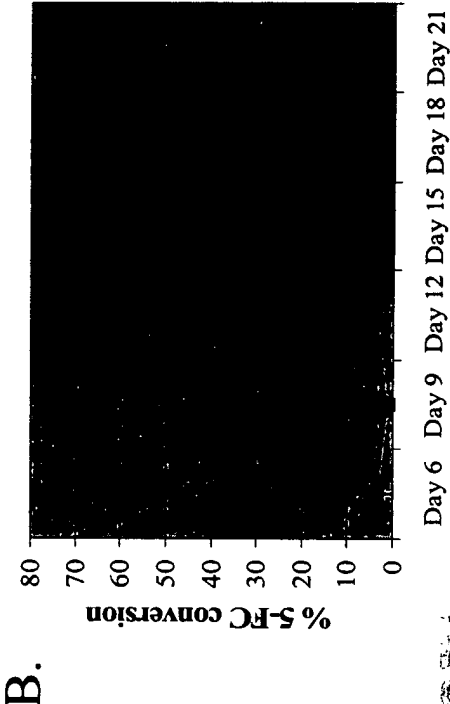
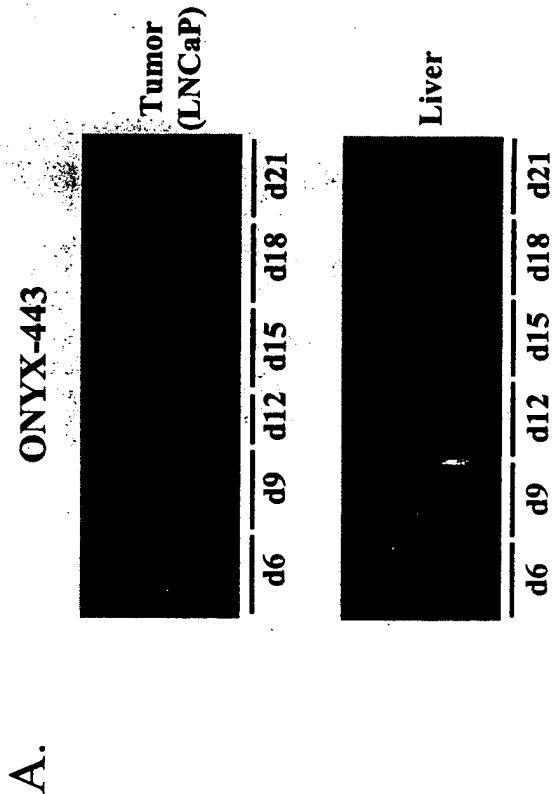
B.

ONYX 443



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Figure 5.



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Figure 6.

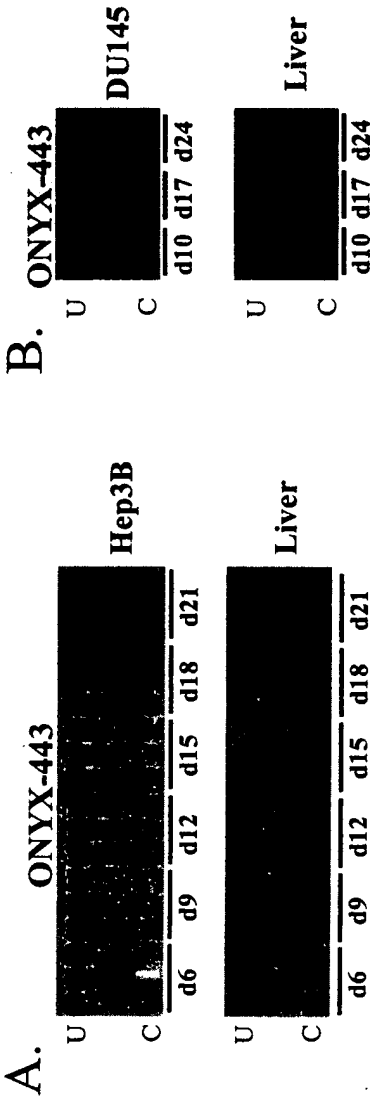


Figure 7. Genomic changes in ONYX-4XX. ITR: inverted terminal repeat; ψ : Viral packaging sequence; E2F1P: E2F1 promoter; H: Hind III site; B: BamH I site; X: Xho I site; S: Spe I site.

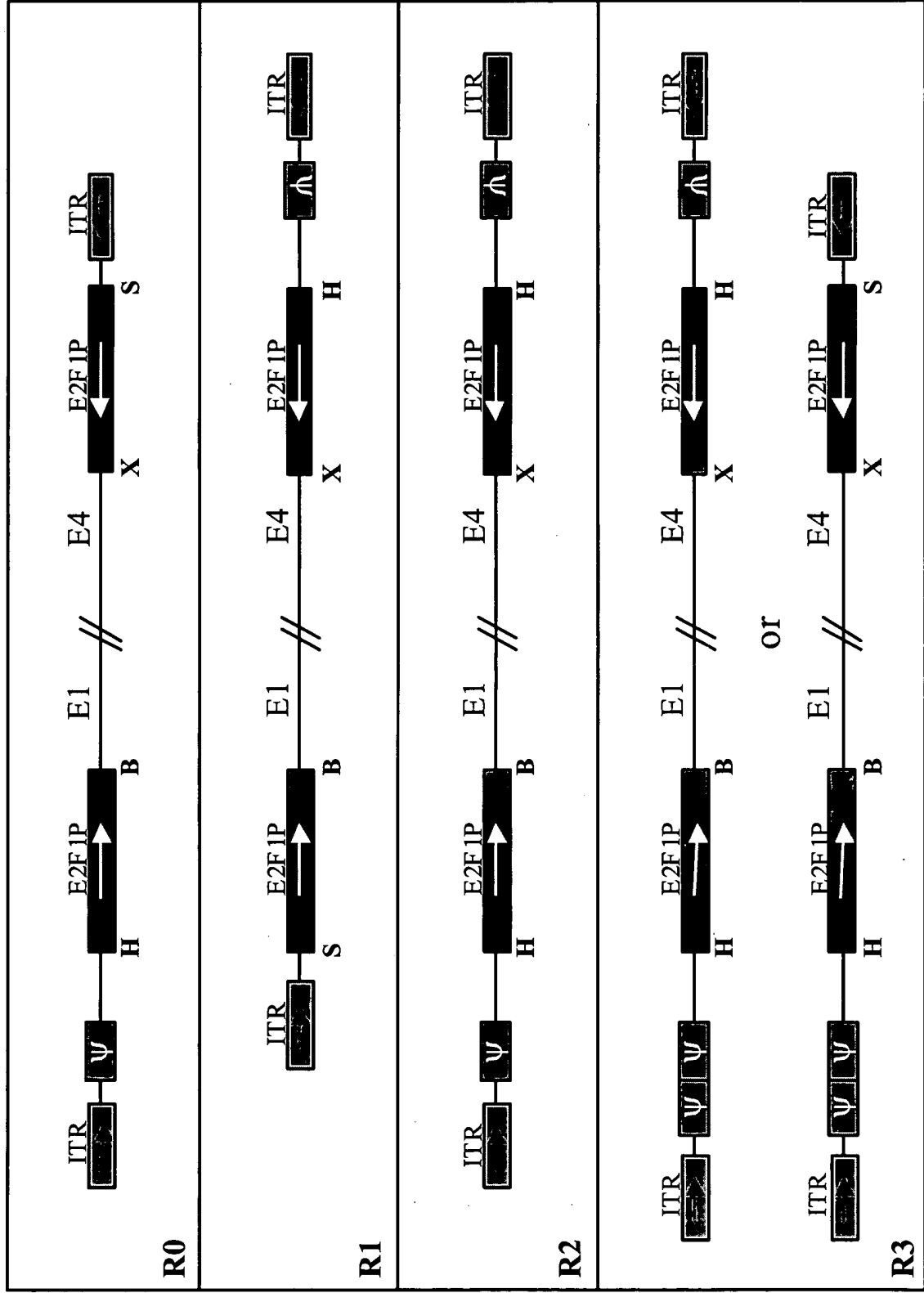
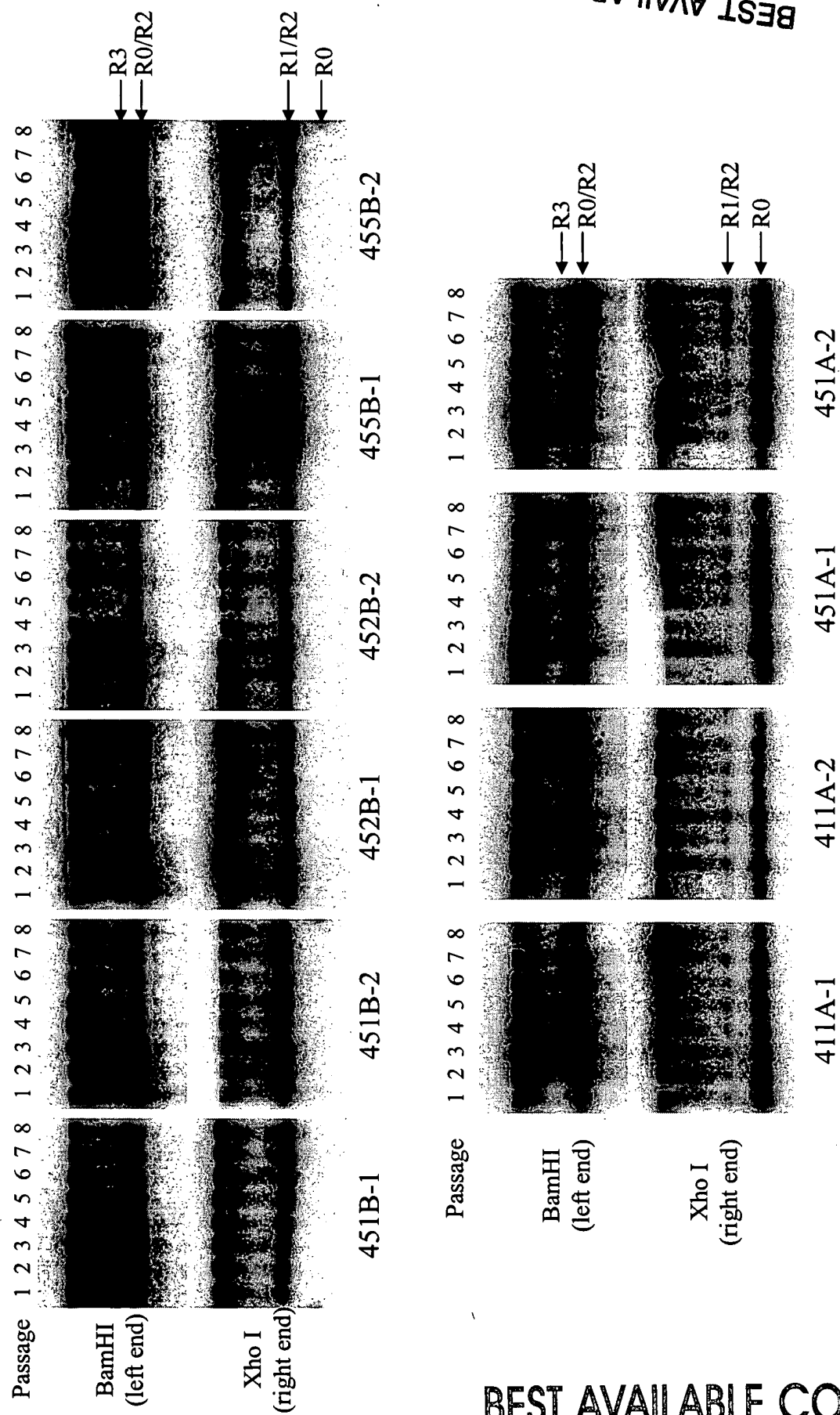


Figure 8. Sequencing Confirmation of ONYX-4XX R2 Termini

1	10	20	30	40	50	60	70	80	Wild type ad5 left end
1	CATCATCAATAATATACCTTAATTTGGATTGAAGCCCAATATGATTAATGAGGGGTGGAGTTTGTGAAGTGGCGCGGGCGG								ONYX-4XX-R2 left end
1	CATCATCAATAATATACCTTAATTTGGATTGAAGCCCAATATGATTAATGAGGGGTGGAGTTTGTGAAGTGGCGCGGGCGG								ONYX-4XX-R2 right end
81	90	100	110	120	130	140	150	160	Wild type ad5 left end
65	TGGGAAACGGGGCGGGTGAAGTGTAGTGTGGGGAAGTGTGATGTGCAAGTGTGGGGAACACATGTAAAGCCGACGATG								ONYX-4XX-R2 left end
65	TGGGAAACGGGGCGGGTGAAGTGTAGTGTGGGGAAGTGTGATGTGCAAGTGTGGGGAACACATGTAAAGCCGACGATG								ONYX-4XX-R2 right end
161	170	180	190	200	210	220	230	240	Wild type ad5 left end
145	TGGCAAAAGTGAACGTTTGTGGTGTGGCGGGTGTACACAGGAAGTGAACAATTTTCGGCGGTTTGTAGGCGGATGTGTAG								ONYX-4XX-R2 left end
145	TGGCAAAAGTGAACGTTTGTGGTGTGGCGGGTGTACACAGGAAGTGAACAATTTTCGGCGGTTTGTAGGCGGATGTGTAG								ONYX-4XX-R2 right end
241	250	260	270	280	290	300	310	320	Wild type ad5 left end
225	TAAATTTGGGCGGTAAACCGAGTAAGATTTGGCCCAATTTTCGGGGGAAAACCTGAATAAGAGGAAGTGAATACTTGAATAATTTT								ONYX-4XX-R2 left end
225	TAAATTTGGGCGGTAAACCGAGTAAGATTTGGCCCAATTTTCGGGGGAAAACCTGAATAAGAGGAAGTGAATACTTGAATAATTTT								ONYX-4XX-R2 right end
321	330	340	350	360	370	380	390	400	Wild type ad5 left end
305	GTGTTACTCATAGCGCGTAATAATTTGTCTAGGGCGCGGGAACCTTGTACCGTTTACGTGGAGACTCGCCAGGTGTTTTT								ONYX-4XX-R2 left end
305	GTGTTACTCATAGCGCGTAATAATTTGTCTAGGGCGCGGGAACCTTGTACCGTTTACGTGGAGACTCGCCAGGTGTTTTT								ONYX-4XX-R2 right end

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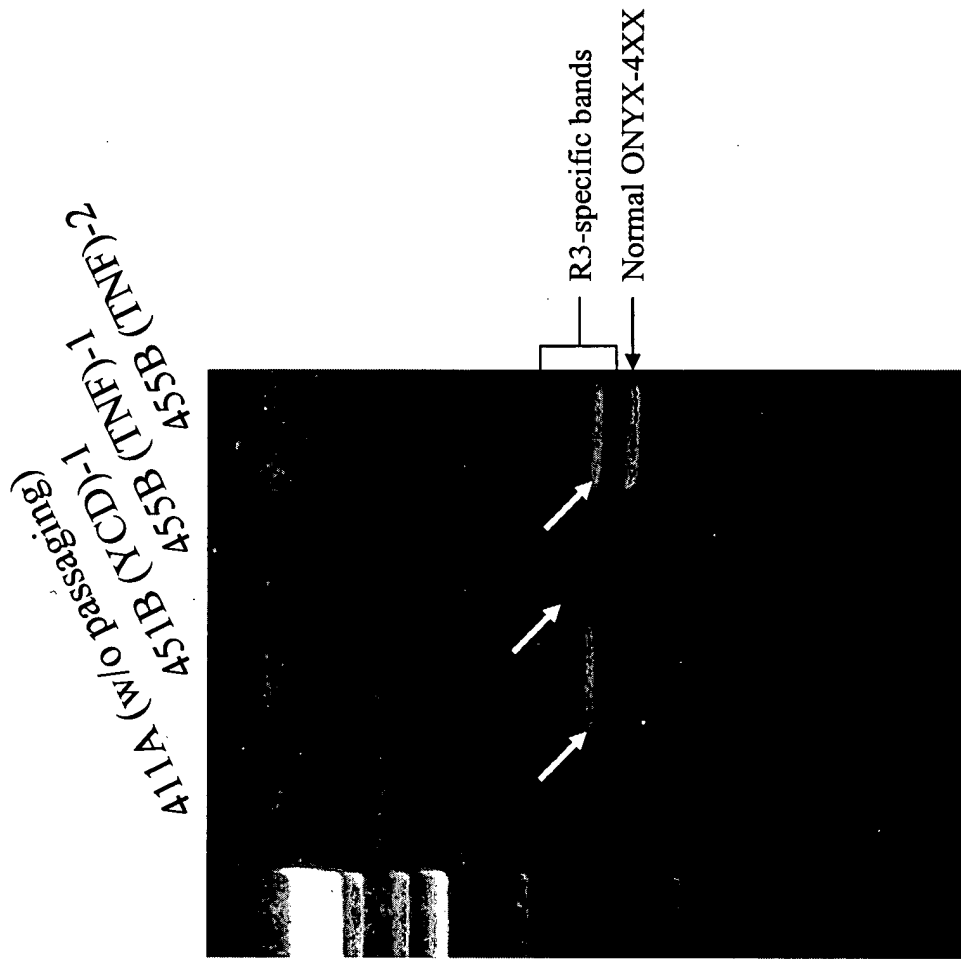
Figure 9 Southern Analysis of Viruses from Serial Passaging



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Figure 10. PCR Analysis of New Species



PCR with P3/P5

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Figure 11. Duplication of Packaging Sequence

1 -----GTGTAGTAAATTTCGG 107 bp YCD1.SEQ
1 -----TGTGTAGTAAATTTCGG 115 bp TNF2.SEQ
1 GAGTTTTTGGTGGCGGTTGACACAGGAAGTGCACAATTTTGGCGGGTTTAGCGCGGATGTGTAGTAAATTTCGG 202 bp TNF1.SEQ
1 -----GGTGTACACAGGAAGTGCACAATTTTGGCGGGTTTAGCGCGGATGTGTAGTAAATTTCGG Ad5 packaging seq

AI

18 CGTAACCGAGTAAGATTTCGCCAATTTTCGGGGAAAACTGAATTAAGAGGAAGTGAATCTGAATAATTTCGTGTACICA 107 bp YCD1.SEQ
19 CGTAACCGAGTAAGATTTCGCCAATTTTCGGGGAAAACTGAATTAAGAGGAAGTGAATCTGAATAATTTCGTGTACICA 115 bp TNF2.SEQ
81 CGTAACCGAGTAAGATTTCGCCAATTTTCGGGGAAAACTGAATTAAGAGGAAGTGAATCTGAATAATTTCGTGTACICA 202 bp TNF1.SEQ
62 CGTAACCGAGTAAGATTTCGCCAATTTTCGGGGAAAACTGAATTAAGAGGAAGTGAATCTGAATAATTTCGTGTACICA Ad5 packaging seq

AII

AIII

AIV

98 TAGCGCGGTAA
99 TAGCGCGTAATAATTGT
161 TAGCGCGTAATAATTGTCTAGGCGCGCGGCGGACATTTCACCGT
142 TAGCGCGTAATAATTTCCTAGGCGCGCGCGGCGGACATTTCAGGCGGACT
107 bp YCD1.SEQ
115 bp TNF2.SEQ
202 bp TNF1.SEQ
Ad5 packaging seq

AV

AVI

AVII

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